

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Attorney Docket No: 37697-0062

Applicant(s): Edward W. MERRILL *et al.* Confirmation No.: 5033
Serial No.: 10/197,263 Examiner: Susan W. BERMAN
Filing Date: July 18, 2002 Group Art Unit: 1711
Title: RADIATION AND MELT TREATED ULTRA HIGH MOLECULAR WEIGHT POLYETHYLENE PROSTHETIC DEVICES

DECLARATION UNDER 37 C.F.R § 1.131

THIS DECLARATION IS TO BE MAINTAINED UNDER THE LIMITED ACCESS
PROVISIONS OF 37 CFR § 1.612; MPEP § 2309.03

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We, Edward W. Merrill, William H. Harris, Premnath Venugopalan, Murali Jasty, Charles R. Bragdon, and Daniel O. O'Connor, do hereby declare as follows:

1. We understand that the claims in the captioned application have been rejected over U. S. patent No. 6,281,264, which lists January 20, 1995 as the earliest filing date.
2. We submit this declaration, based on our personal knowledge to explain the process leading to the inventions disclosed in U. S. application Serial No. 10/197,263 that relate to orthopedic preformed materials and polymers, articles and the like that comprise polymers cross-linked by irradiation and heated to or above the melting point of the polymer, and methods of making same.
3. Wear of polyethylene and the incidence of osteolysis became known during mid-1980's. The realization was that the osteolysis was related to the formation of very small polyethylene particles through wear. In order to improve wear resistance of polyethylene and to prevent the formation of fine polyethylene particles, we carried out inventive activities and designed and carried out various experiments prior to January 20, 1995. All dates on the attached Exhibits have been masked out.

Cross-linking by Irradiation in a Molten State to lower crystallinity and Preserve the Entangled State

4. Prior to January 20, 1995, we developed several ideas to lower crystallinity and preserve the highly disordered entangled state of the ultra-high molecular weight polyethylene (UHMWPE) in order to solve the wear problem (see Exhibit 1). One embodiment that we developed was to cross-link the polyethylene in the molten state by use of irradiation so that the polyethylene could not revert readily to the chain folded state, which was preferred at the time. This embodiment is memorialized in item C of Exhibit 1. The process also is disclosed in U.S. Serial No. 08/600,744, filed February 13, 1996, and issued as U.S. Patent No. 5,879,400 (the '400 patent) (see, for example, Column 6, lines 55-67, and Example 1), U.S. Serial No. 08/726,313 (the '313 application, filed October 2, 1996) (see, for example, page 25, Example 1), and U.S. Serial No. 08/798,638 (the '638 application, filed February 11, 1997) (see, for example, pages 33-34 , Example 1).

5. Prior to January 20, 1995, we conceived of various embodiments of the invention, that is irradiation of UHMWPE combined with melting, as described in item C of Premnath Venugopalan's note (see Exhibit 1). At the time, we believed that a prosthesis formed out of UHMWPE bar stock that had been heated above the melting point and irradiated (in air or an inert environment) in that molten state (see item c), or had been irradiated and then heated above the melting point, would form cross-links (see item b). The increased mobility of the molecules in the molten state allows the free radicals to combine with each other and form cross-links, as opposed to remaining in a trapped state.

6. Prior to January 20, 1995, we continued conducting melt-irradiation (MIR) experiments at Mr. Kenneth Wright's laboratory (the High Voltage Research Laboratory (HVRL), located in building N-10 of M.I.T. at 155 Massachusetts Avenue, Cambridge, MA 02139. Mr. Kenneth Wright was responsible for the day-to-day operation and management of the radiation applications activities of the HVRL, including scheduling, operation, maintenance of equipment and research with the Van de Graaff

accelerators). Six UHMWPE samples were irradiated at 1.0, 2.5, 5, 10, 20 and 50 Mrads by Mr. Ken Wright. The samples were heated to melt and irradiated while in a molten state. Subsequently, MIR experiments using solid bars in sealed containers (sealed glass vials) were done at Mr. Wright's laboratory. Copies of Mr. Wright's laboratory logbook page numbers 122-123 and 126-127 containing the record of MIR work done are attached as Exhibit 2. A copy of the corresponding page 10 of lab book no. 2 is attached as Exhibit 3.

7. Also, prior to January 20, 1995, we conducted a thermal analysis of the irradiated UHMWPE specimens, as described in paragraph 9, by use of DSC. This DSC method is used to determine melting and crystallization temperatures as well as the energy input required to melt and energy output generated during crystallization. The energy required to melt is then used to quantify the degree of crystallinity.

Six polymer samples, as described in paragraph 9, also were irradiated in sealed pans for crystallinity analysis. The samples were heated to melt and irradiated while in a molten state. A copy of Premnath Venugopalan's laboratory note book page numbers 8-9 is attached as Exhibit 3 (see Expt 1 and Expt 2). Thus, prior to January 20, 1995, we have practiced the process of heating polyethylene to a temperature at or above the melting point of polyethylene and irradiating the polyethylene in a molten state. The DSC testing on the polyethylene samples that were irradiated in a molten state was conducted. Crystallinity levels had dropped to 37.77% (printed as 37.8%) for the sample given a 20 Mrad radiation dose. Copies of the corresponding DSC data sheets are attached as Exhibit 4 (marked as 'data-6'). Crystallinity data from unirradiated GUR415 bar stock was used as control. Irradiation dose (20 Mrad), temperature (125.51, printed as 125.5) and crystallinity data (37.77%, printed as 37.8%) from this work are presented in a patent application that became the '400 patent (see, for example, Table 1 on column 9 of the '400 patent), in the '313 application (see, for example, Table 1, page 27), and the '638 application (see, for example, Table 1, page 35).

8. Other tests on melt-irradiated polyethylene, for example, Electron Spin Resonance (ESR), were conducted to determine residual free radicals. Swell Ratios to assess degree of cross-linking also were determined, prior to January 20, 1995, by submerging polyethylene in Decalin™ at 150°C for dissolution of polymeric chains.

ESR results indicated no detectable free radicals in melt-irradiated polyethylene, whereas the control polyethylene that was irradiated at room temperature without concurrent or subsequent melting showed the presence of free radicals. The absence of free radicals in the melt-irradiated polyethylene indicates that any further oxidative degradation would be avoided, and thus the material was suitable for use in medical prostheses. See Exhibit 5 for ESR spectra from an experiment conducted prior to January 20, 1995. The ESR spectra show samples irradiated at room temperature contain free radicals; whereas, the samples irradiated at 175°C do not have any detectable free radicals.

Swell Ratios indicated that the melt-irradiated polyethylene was highly crosslinked and did not allow dissolution of polymeric chains, while unirradiated polyethylene dissolved completely, which signifies lack of cross-linking in the unirradiated polyethylene. See Exhibit 6 for swell test results of an experiment conducted prior to January 20, 1995. Swell test data shows control specimens dissolve completely within 24 hours in Decalin™ at 150°C.

9. The above testing confirmed that we had invented, among other things, (1) methods of making an improved prostheses by combining melting and irradiating to cross-link UHMWPE, and (2) improved prostheses that were the result of these processes. These prostheses are wear resistant and thus would not be a source of the fine particles that would result in bone resorption, as was the case with the prior art conventional UHMWPE prosthesis.

Cross-linking by irradiation at room temperature and subsequent melting

10. Prior to January 20, 1995, we also developed another embodiment to preserve the highly disordered entangled state of the UHMWPE in order to solve the

wear problem (see item b of Exhibit 1). The embodiment involved cross-linking the polyethylene in at room temperature ('cold irradiation') by irradiation and subsequent melting. The process is referred to as Cold-irradiation and Subsequent Melting or "CISM" and is disclosed in U.S. Serial No. 08/726,313 (the '313 application, filed October 2, 1996) (see, for example, page 39, Example 8), and U.S. Serial No. 08/798,638 (the '638 application, filed February 11, 1997) (see, for example, pages 47-48 , Example 8).

11. According to this embodiment, UHMWPE is irradiated at room temperature to cross-link and subsequently the irradiated UHMWPE is heated above the melting point of about 135°C and then cooled. This process subsequently referred to as cold irradiation and subsequent melting or "CISM", meaning irradiation of UHMWPE at about room temperature and then heating the irradiated UHMWPE above the melting point and resolidifying.

12. Prior to January 20, 1995, we had a number of UHMWPE specimens irradiated at room temperature at Mr. Kenneth Wright's laboratory. A copy of Mr. Wright's laboratory logbook pages number 120-121 containing a log of irradiation work done prior to January 20, 1995 is attached as Exhibit 2. The experiment (Marked as Irradiation Experiment 1) and the process including radiation doses used are recorded in lab note book no. 2, page no. 8. A copy of the laboratory note book page number 8, which is attached as Exhibit 3.

13. Prior to January 20, 1995, we conducted a thermal analysis of the room-temperature irradiated UHMWPE specimens, as described in paragraph 11, by use of a testing method called differential scanning calorimetry ("DSC"). This DSC method is used to determine melting and crystallization temperatures as well as the energy input required to melt and energy output generated during crystallization. The energy required to melt is then used to quantify the degree of crystallinity. This DSC method generally has two heating-cooling cycles during which the energy input and output is measured. The cycles include of heating the specimen to a temperature above its melting point, cooling down to room temperature, and heating again to a temperature

above its melting point. The first cycle of this DSC method, involved heating and cooling, was applied to the room temperature irradiated UHMWPE test specimens, as described in paragraph 10 above. Therefore, we practiced the "CISM" process prior to January 20, 1995. The DSC test results indicated that the crystallinity levels decreased from approximately 54.71% present in the starting material to as low as 41.69% when irradiated at 20 Mrad. A copy of that data sheet is attached as Exhibit 4 (see sheet marked as 'data-4') and the corresponding DSC data sheet is attached as Exhibit 4. This reduced crystallinity confirmed our view that the "CISM" method also would improve the structure and wear resistance of the UHMWPE by decreasing the content of chain-folded crystalline lamellae, which otherwise would lead to fibril formation.

The above testing confirmed that we had developed (1) methods of making improved prostheses using the CISM method to cross-link UHMWPE, and (2) improved prostheses that were the result of the process. These prostheses would not be a source of the fine particles that would result in bone resorption as was the case with the prior art UHMWPE prosthesis. Subsequent testing also confirmed that the elimination of free radicals was provided by this method. Thus, prior to January 20, 1995, we conceived and reduced to practice the CISM invention, that is irradiation of UHMWPE at room temperature and subsequent melting, as described in item b of Exhibit 1.

14. The above testing confirmed that we had invented, among other things, (1) methods of making an improved medical implant having bearing surface comprising a solid polyethylene by irradiating to cross-link UHMWPE and subsequent melting, and (2) improved medical implants. This medical implant would be wear resistant and thus would not be a source of the fine particles that would result in bone resorption, as was the case with the prior art conventional UHMWPE prosthesis.

We hereby declare that all statements made herein of our own knowledge are true, and that all statements made on information and belief are believed to be true; and further, that these statements are made with the knowledge that willful false statements, and the like so made, are punishable by fine or imprisonment, or both,

under Section 1001, Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

April 14, 2004

Date

Edward W. Merrill

Edward W. Merrill

Date

William H. Harris

Date

Premnath Venugopalan

Date

Murali Jasty

Date

Charles R. Bragdon

Date

Daniel O. O'Connor